REMARKS

Claim 1 has been amended to clearly point out and distinctly claim what Applicant regards as the subject matter of the present invention. Claim 1 has been amended to recite that systemic host defense mechanisms are stimulated and incorporates the limitation of canceled claim 6.

Objection to Claims 13 and 14 under 37 CFR §1.75(b)

Claims 13 and 14 stand objected to under 37 CFR §1.75(b) as allegedly being duplicate claims. Claim 13 is drawn to a method that uses an interferon comprising a Type II interferon. Claim 14 further limits the Type II interferon to a gamma-interferon. The Examiner alleges that Type II and gamma interferons are the same genus. Applicant respectfully disagrees. Type II interferons comprise the genus and the gamma interferon is the species. As noted in our previous response, the possibility that there may exist other Type II interferons should not be precluded. Subsequent discovery of another Type II interferon would not be covered if Applicant canceled claim 13. In an infringement action, equivalents are determined at the time of infringement; Applicant believes that the genus, Type II interferon, is broader than the species, gamma interferon, because there can be more than one species encompassed by the genus. If Applicant were required to choose one claim over the other it would be to their detriment. Thus, Applicant is entitled to both the broad and narrow claims. Therefore, Applicant believes that claims 13 and 14 are in fact different in scope and content and should not be required to surrender subject matter. Applicant respectfully requests that the objection be withdrawn.

The Cited Art

The Examiner has cited three references against the instant application. Before addressing the rejections individually, a summary of the teachings from the cited art will be presented. The three references are (1) U.S. Patent No. 5,019,382 by Cummins ("Cummins"); (2) J. Infect. Dis. 150:181-188 (1984) by Samo et al. ("Samo"); and (3) Vaccine 7:229-233 (1989) by Iida et al. ("Iida").

Cummins: The Cummins reference teaches the administration of very low dose (0.01 to 5 IU/lb) interferon for the treatment of various disease states. The disease conditions in humans treated with interferon were all non-viral (i.e., rheumatoid arthritis, multiple sclerosis, lymphoma, mesothelioma, apthous stomatitis and acne). For data on the treatment of viral

conditions Cummins presents data from cats and dogs. The interferon is administered orally using different regimens. The first set of clinical data shows that human alpha interferon is superior to bovine beta-interferon in prolonging survival times for infected animals. However, there is no indication that the treatment afforded any benefit over no treatment for the canine parvovirus disease nor that an increased dose would be desirable.

The efficacy of interferon in canine herpesvirus (CHV) inoculated puppies was assessed in a series of experiments. It is interesting to note that when various doses were compared that either no benefit from treatment at any dosage was seen (see Litter 2; Col. 10, line 5) or that the higher dosage did not provide a survival benefit over the lower dosage, but instead pups given the higher dosage died, on average, one day sooner. See Litter 1; Column 9, lines 55-59. Thus, Cummins teaches away from using a higher dose interferon treatment.

Samo: Samo teaches the treatment of a local infection via the direct application of interferon to the site of infection. Samo prophylactically treats a human with intranasal (not oromucosal) interferon administration, then infects the human with an intranasal rhinovirus challenge. Samo fails to teach treatment after infection has occurred or the treatment of a non-localized infection.

Iida: Iida teaches intranasal interferon-γ administration for the prophylactic treatment of viral infections, i.e., Iida teaches that the interferon must be administered prior to infection to be efficacious. See page 230. Iida teaches the treatment of a local infection via the direct application of interferon to the site of infection (intranasal Sendai influenza viral infection). Iida also teaches that subcutaneous interferon administration was ineffective against viruses that have been introduced at a site other than the nasal passageways (intravenous injection of herpes simplex virus type I). Iida fails to teach the oromucosal administration of interferon for the treatment of systemic infections.

Rejections under 35 USC §102(b)

In order to anticipate a prior art reference must contain within the four corners of the document all the functional and quantitative limitations of the claimed invention. The presently claimed invention is directed to the oromucosal administration of an interferon in an amount that provides effective treatment of a disease without inducing a pathological response. It is a critical aspect, and one not found in the prior art, that oromucosal interferon administration is an effective

treatment for non-local infections. Thus, in order to fully anticipate, a prior art reference must contain the following elements for the method claims: 1) oromucosal interferon administration; 2) of a therapeutically effective amount; 3) without a pathological response; 4) in dosages from about 21.4 IU/kg to about 2.9 x 10^4 IU/kg; for stimulating systemic host defense mechanism. In order to fully anticipate a prior art reference must contain the following elements for the composition claims: 1) a unit dosage form; 2) comprising a therapeutically effective amount from about 1500 IU to about 20 x 10^6 IU interferon; 3) suitable for oromucosal administration.

Claims 1, 2, 4, 5, 10, and 11

Claims 1, 2, 4, 5, 10, and 11 stand rejected under 35 USC §102(b) as being anticipated by Cummins (U.S. Patent 5, 019,382). Claims 1, and 2 are independent claims; claims 4, 5, 10 and 11 are dependent claims and depend from claim 1. The Examiner equates the 0.7 IU/lb doses with the "lesser amounts" of the instant claims. However, Applicant notes that only dependent Claim 4 contains language to "lesser amounts." As this rejection applies to Claim 4, the largest cumulative dose used in Cummins for the treatment of a viral disease condition would be 140 IU (10 IU x 2 doses/day x 7 days). Applicant notes that this is well below the claimed dosages in the instant application.

Additionally, the Examiner alleges that Cummins meets all of the functional and quantitative limitations of the claims. Applicant respectfully disagrees. Cummins, as noted above, fails to teach the administration of interferon (1) at a dose from about 21.4 IU/kg to about 2.9 x 10^4 IU/kg. Without these teachings Cummins cannot anticipate the presently claimed invention. Thus, the Cummins patent is not good anticipatory art.

Claims 1-8, 10-12 and 15-18

Claims 1-8, 10-12 and 15-18 stand rejected under 35 USC §102(b) as being anticipated by Samo *et al.* Samo teaches the intranasal administration of either 0.7 x 10^6 or 2.4 x 10^6 units of interferon for the treatment of a local rhinovirus infection. Samo prophylactically applies the interferon to the tissue that will be the site of infection, i.e., the nose, not the oromucosa. Thus, Samo fails to teach the application of interferon for the treatment of an existing viral infection as is presently claimed. For the foregoing reasons, Samo fails to anticipate the claimed invention.

Claims 1-3, 5 and 13-14

Claims 1-3, 5 and 13-14 stand rejected under 35 USC §102(b) as being anticipated by Iida *et al.* For the reasons noted above for the rejection based on Samo, Iida also fails to anticipate the claimed invention because there is no indication that the intranasal application of interferon has therapeutic effects removed from the application site. Further, as applied to Claim 2, Iida fails to show any benefit if the interferon is administered after infection, even for a localized nasal infection of rhinovirus. Thus, for the foregoing reasons, Iida fails to anticipate the claimed invention.

Rejection under 35 USC §103(a)

Initially, Applicants note that the test for non-obviousness articulated by the Court of Appeals for the Federal Circuit requires that the combination of the teachings of all or any of the references would have suggested the possibility of further improvement by combining such teachings. Thus, both the suggestion and reasonable expectation of success must be founded in the prior art, not in the Applicant's disclosure. *See* In re Vaeck, 20 USPQ2d 1439 (Fed Cir. 1991).

Claim 9

Claim 9 remains rejected under 35 USC §103(a) as being unpatentable over Iida *et al.* Claim 9 depends from Claim 1 and further comprises the co-administration of other cytokines or interferon inducers. As stated above, Iida fails to disclose the use of interferon oromucosally in an amount claimed by Applicants for the systemic stimulation of host defense mechanism. Further, Iida fails to provide any motivation for the co-administration of other cytokines or interferon inducers. It is the prior art, and not the Applicant's disclosure, that must establish the obviousness of the combination. Additionally, the essence of the Examiner's argument is that it would be obvious to try the combination of IFN with other cytokines. However, obvious to try is not the standard by which obviousness is measured. The prior art must provide the motivation to make and/or use the combination.

The Examiner has cited *In re Kerkhoven* in support of his position. First, Applicant notes that the use of interferon in the present invention is not for the same purpose as Iida, which is required by Kerkhoven. Second, Applicant draws the Examiner's attention to *In re Geiger*, 815

F.2d 686, 2 USPQ2d 1276 (Fed. Cir. 1987) which notes that hindsight reconstruction or obvious to try criteria are insufficient.

As noted above, the test for obviousness is that both the suggestion and reasonable expectation of success must be founded in the prior art, not in the Applicant's disclosure. Iida fails to provide the motivation for the claimed method. Therefore, one skilled in the art would not be motivated to co-administer IFN with either other cytokines or interferon inducers via the oromucosal route as presently claimed and, thus, Iida fails to render obvious the method as described by claim 9.

Claims 1-18

Claims 1-18 stand rejected under 35 USC §103(a) as being unpatentable over Cummins in view of either Samo *et al.* or Iida *et al.* The combination of Cummins and Iida *et al.*, or Cummins and Samo *et al.*, is not suggested by either reference. Cummins does not suggest any dose of interferon greater than 4 IU/lb (see Column 8, line 23) should be used. In fact, Cummins typically uses a dose of about 1 IU/lb or less. Furthermore, **Cummins actually teaches away** from using higher doses by noting at Column 9, lines 55-58, "The higher dosage, HAI (10x), *did not provide a survival benefit* over the lower dosage, but instead pup given the *higher dosage died, on the average, one day sooner.*" (Emphasis added.) Thus, a skilled artisan would not be motivated to increase the dosage nor to combine Cummins with any other art. Although Iida uses a high dose, given the known toxicity of interferon in the art, the skilled artisan would not be motivated to increase the dosage. Indeed, Samo *et al.* teaches away from increasing the dose by noting that an increased incidence of adverse side effects is seen with increasing dosages of interferon. See Table 2, at page 186, of the Samo reference. Thus, one skilled in the art would not be motivated to combine Cummins with either Samo or Iida to obtain the claimed invention. Even if combined, there is no teaching of oramucosal administration nor of systemic stimulations of host defense mechanism. Applicant respectfully requests that the rejection be withdrawn.

Conclusion

In view of the foregoing amendments and remarks, Applicant respectfully requests reconsideration and allowance on the merits of all pending claims.

Respectfully submitted,

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